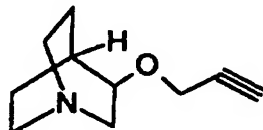




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 31/44	A1	(11) International Publication Number: WO 98/46225 (43) International Publication Date: 22 October 1998 (22.10.98)
<p>(21) International Application Number: PCT/US98/07152</p> <p>(22) International Filing Date: 8 April 1998 (08.04.98)</p> <p>(30) Priority Data: 60/043,570 11 April 1997 (11.04.97) US</p> <p>(71) Applicant (for all designated States except US): ELI LILLY AND COMPANY [US/US]; Lilly Corporate Center, Indianapolis, IN 46285 (US).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): SHANNON, Harlan, Edgar [US/US]; 4229 Rolling Springs Drive, Carmel, IN 46033 (US). WHITESITT, Celia, Ann [US/US]; 4089 Easy Street, Greenwood, IN 46142 (US).</p> <p>(74) Agents: LENTZ, Nelsen, L. et al.; Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285 (US).</p>		<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i></p>

(54) Title: METHOD FOR TREATING SCHIZOPHRENIA



(I)

(57) Abstract

The present invention provides a method for treating a condition selected from the group consisting of schizophrenia, schizoaffective disorder, and schizophreniform disorder in a patient using a Compound (I).

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METHOD FOR TREATING SCHIZOPHRENIA

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This invention provides a method for treating or alleviating the symptoms of pathologic psychosis, comprising administering an effective amount of a cyano-oxime compound.

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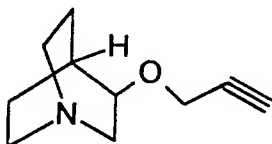
The method of this invention provides a method for treating schizophrenia using compounds which were previously disclosed for use in the treatment of Alzheimer's Disease.

15

The method of this invention provide the clinician with another treatment option for the treatment of psychotic conditions. The compounds used in the presently claimed method appear to have an acceptable side effect profile while providing surprising anti-psychotic activity.

20

The present invention provides a method for treating a condition selected from the group consisting of schizophrenia, schizophreniform disorder, and schizoaffective disorder, comprising administering an effective amount of Compound I:



I

25

or

a pharmaceutically acceptable salt or solvate thereof.

30

The present invention provides a method for treating a pathologic psychotic condition selected from the group consisting of Conduct Disorder, Solitary Aggressive Type (312.00), Conduct Disorder, Undifferentiated Type (312.90), Tourette's Disorder (307.23), Chronic Motor Or Vocal Tic Disorder (307.22), Transient Tic Disorder (307.21), Tic Disorder NOS (307.20), Alcohol Withdrawal

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Delirium (291.00), Alcohol Hallucinosi s (291.30), Alcohol
Dementia Associated with Alcoholism (291.20), Amphetamine or
Similarly Acting Sympathomimetic Intoxication (305.70),
Amphetamine or Similarly Acting Sympathomimetic Delirium
5 (292.81), Amphetamine or Similarly Acting Sympathomimetic
Delusional Disorder (292.11), Cannabis Delusional Disorder
(292.11), Cocaine Intoxication (305.60), Cocaine Delirium
(292.81), Cocaine Delusional Disorder (292.11), Hallucinogen
Hallucinosi s (305.30), Hallucinogen Delusional Disorder
10 (292.11), Hallucinogen Mood Disorder (292.84), Hallucinogen
Posthallucinogen Perception Disorder (292.89), Phencyclidine
(PCP) or Similarly Acting Arylcyclohexylamine Intoxication
(305.90), Phencyclidine (PCP) or Similarly Acting
Arylcyclohexylamine Delirium (292.81), Phencyclidine (PCP)
15 or Similarly Acting Arylcyclohexylamine Delusional Disorder
(292.11), Phencyclidine (PCP) or Similarly Acting
Arylcyclohexylamine Mood Disorder (292.84), Phencyclidine
(PCP) or Similarly Acting Arylcyclohexylamine Organic Mental
Disorder NOS (292.90), Other or Unspecified Psychoactive
20 Substance Intoxication (305.90), Other or Unspecified
Psychoactive Substance Delirium (292.81), Other or
Unspecified Psychoactive Substance Dementia (292.82), Other
or Unspecified Psychoactive Substance Delusional Disorder
(292.11), Other or Unspecified Psychoactive
25 SubstanHallucinosi s (292.12), Other or Unspecified
Psychoactive Substance Mood Disorder (292.84), Other or
Unspecified Psychoactive Substance Anxiety Disorder
(292.89), Other or Unspecified Psychoactive Substance
Personality Disorder (292.89), Other or Unspecified
30 Psychoactive Substance Organic Mental Disorder NOS (292.90),
Delirium (293.00), Dementia (294.10), Organic Delusional
Disorder (293.81), Organic Hallucinosi s (293.82), Organic
Mood Disorder (293.83), Organic Anxiety Disorder (294.80),
Organic Personality Disorder (310.10), Organic Mental
35 Disorder (294.80), Obsessive Compulsive Disorder (300.30),
Post-traumatic Stress Disorder (309.89), Generalized Anxiety
Disorder (300.02), Anxiety Disorder NOS (300.00), Body

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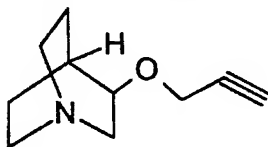
Dysmorphic Disorder (300.70), Hypochondriasis (or Hypochondriacal Neurosis) (300.70), Somatization Disorder (300.81), Undifferentiated Somatoform Disorder (300.70), Somatoform Disorder NOS (300.70), Intermittent Explosive Disorder (312.34), Kleptomania (312.32), Pathological Gambling (312.31), Pyromania (312.33), Trichotillomania (312.39), and Impulse Control Disorder NOS (312.39);

Schizophrenia, Catatonic, Subchronic, (295.21), Schizophrenia, Catatonic, Chronic (295.22), Schizophrenia, Catatonic, Subchronic with Acute Exacerbation (295.23), Schizophrenia, Catatonic, Chronic with Acute Exacerbation (295.24), Schizophrenia, Catatonic, in Remission (295.55), Schizophrenia, Catatonic, Unspecified (295.20), Schizophrenia, Disorganized, Subchronic (295.11), Schizophrenia, Disorganized, Chronic (295.12), Schizophrenia, Disorganized, Subchronic with Acute Exacerbation (295.13), Schizophrenia, Disorganized, Chronic with Acute Exacerbation (295.14), Schizophrenia, Disorganized, in Remission (295.15), Schizophrenia, Disorganized, Unspecified (295.10), Schizophrenia, Paranoid, Subchronic (295.31), Schizophrenia, Paranoid, Chronic (295.32), Schizophrenia, Paranoid, Subchronic with Acute Exacerbation (295.33), Schizophrenia, Paranoid, Chronic with Acute Exacerbation (295.34), Schizophrenia, Paranoid, in Remission (295.35), Schizophrenia, Paranoid, Unspecified (295.30), Schizophrenia, Undifferentiated, Subchronic (295.91), Schizophrenia, Undifferentiated, Chronic (295.92), Schizophrenia, Undifferentiated, Subchronic with Acute Exacerbation (295.93), Schizophrenia, Undifferentiated, Chronic with Acute Exacerbation (295.94), Schizophrenia, Undifferentiated, in Remission (295.95), Schizophrenia, Undifferentiated, Unspecified (295.90), Schizophrenia, Residual, Subchronic (295.61), Schizophrenia, Residual, Chronic (295.62), Schizophrenia, Residual, Subchronic with Acute Exacerbation (295.63), Schizophrenia, Residual, Chronic with Acute Exacerbation (295.94), Schizophrenia, Residual, in Remission (295.65), Schizophrenia, Residual,

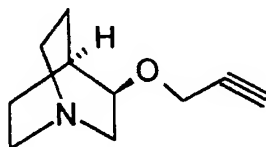
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Unspecified (295.60), Delusional (Paranoid) Disorder (297.10), Brief Reactive Psychosis (298.80), Schizophreniform Disorder (295.40), Schizoaffective Disorder (295.70), Induced Psychotic Disorder (297.30), Psychotic Disorder NOS (Atypical Psychosis) (298.90), Personality Disorders, Paranoid (301.00), Personality Disorders, Schizoid (301.20), Personality Disorders, Schizotypal (301.22), Personality Disorders, Antisocial (301.70), and Personality Disorders, Borderline (301.83) comprising administering an effective amount of Compound I or a pharmaceutically acceptable salt thereof.

As noted hereinbefore, the quinuclidine compound referred to herein as Compound I, employed in the method of the present invention is known. The compound, methods of preparing the compounds, as well as pharmaceutical formulations containing the compounds, are disclosed in issued United States Patent number 5,286,864 issued on February 15, 1994, herein incorporated by reference in its entirety. Thus, the artisan can readily prepare the Compound I materials described herein using the teachings in the published patent applications. To further clarify, Compound I shall refer to a compound of the structure:



or
a pharmaceutically acceptable salt or solvate thereof. A particularly preferred Compound I is of the formula II:



II

An especially preferred compound is known as
WAL 2014.

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5 The term "psychotic condition" refers to a condition wherein hallucinations, delusions, and/or confused thought process are characteristic manifestations of the named condition.

 The term "pathologic" refers to a clinically significant disease state.

10 The term "effective amount", as used herein, represents an amount of compound necessary to prevent or treat a human susceptible to or suffering from a psychotic condition following administration to such human. The active compound is effective over a wide dosage range. For example, dosages per day will normally fall within the range
15 of about 0.005 to about 500 mg/kg of body weight. In the treatment of adult humans, the range of about 0.05 to about 100 mg/kg, in single or divided doses, is preferred. However, it will be understood that the amount of the compound actually administered will be determined by a
20 physician, in the light of the relevant circumstances including the condition to be treated, the choice of compound to be administered, the age, weight, and response of the individual patient, the severity of the patient's symptoms, and the chosen route of administration, and
25 therefore the above dosage ranges are not intended to limit the scope of the invention in any way.

 The compound may further be delivered by a variety of other pharmaceutically accepted routes including, but in no way limited to parenterally, subcutaneous, intranasal,
30 intramuscular and intravenous routes. Such formulations may be designed to provide delayed or controlled release using formulation techniques which are known in the art.

 As used herein the term "treating" includes prophylaxis of a physical and/or mental condition or
35 amelioration or elimination of the developed physical and/or mental condition once it has been established or alleviation of the characteristic symptoms of such condition.

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Pathologic psychological conditions which are psychoses or may be associated with psychotic features include, but are not limited to the following disorders which have been characterized in the DSM-III-R.

5 Diagnostic and Statistical Manual of Mental Disorders, Revised, 3rd Ed. (1980). The DSM-III-R was prepared by the Task Force on Nomenclature and Statistics of the American Psychiatric Association, and provides clear descriptions of diagnostic catagories. The numbers in
10 parenthesis refer to the DSM-III-R categories. The skilled artisan will recognize that there are alternative nomenclatures, nosologies, and classification systems for pathologic psychological conditions and that these systems evolve with medical scientific progress.

15 Examples of pathologic psychologic conditions which may be treated using Compound I include, but are not limited to, Conduct Disorder, Solitary Aggressive Type (312.00), Conduct Disorder, Undifferentiated Type (312.90), Tourette's Disorder (307.23), Chronic Motor Or
20 Vocal Tic Disorder (307.22), Transient Tic Disorder (307.21), Tic Disorder NOS (307.20), Alcohol Withdrawal Delirium (291.00), Alcohol Hallucinosiis (291.30), Alcohol Dementia Associated with Alcoholism (291.20), Amphetamine or Similarly Acting Sympathomimetic Intoxication
25 (305.70), Amphetamine or Similarly Acting Sympathomimetic Delirium (292.81), Amphetamine or Similarly Acting Sympathomimetic Delusional Disorder (292.11), Cannabis Delusional Disorder (292.11), Cocaine Intoxication (305.60), Cocaine Delirium (292.81), Cocaine Delusional
30 Disorder (292.11), Hallucinogen Hallucinosiis (305.30), Hallucinogen Delusional Disorder (292.11), Hallucinogen Mood Disorder (292.84), Hallucinogen Posthallucinogen Perception Disorder (292.89), Phencyclidine (PCP) or Similarly Acting Arylcyclohexylamine Intoxication
35 (305.90), Phencyclidine (PCP) or Similarly Acting Arylcyclohexylamine Delirium (292.81), Phencyclidine (PCP) or Similarly Acting Arylcyclohexylamine Delusional

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Disorder (292.11), Phencyclidine (PCP) or Similarly
Acting Arylcyclohexylamine Mood Disorder (292.84),
Phencyclidine (PCP) or Similarly Acting
Arylcyclohexylamine Organic Mental Disorder NOS (292.90),
5 Other or Unspecified Psychoactive Substance Intoxication
(305.90), Other or Unspecified Psychoactive Substance
Delirium (292.81), Other or Unspecified Psychoactive
Substance Dementia (292.82), Other or Unspecified
Psychoactive Substance Delusional Disorder (292.11),
10 Other or Unspecified Psychoactive SubstanHallucinosi
(292.12), Other or Unspecified Psychoactive Substance
Mood Disorder (292.84), Other or Unspecified Psychoactive
Substance Anxiety Disorder (292.89), Other or Unspecified
Psychoactive Substance Personality Disorder (292.89),
15 Other or Unspecified Psychoactive Substance Organic
Mental Disorder NOS (292.90), Delirium (293.00), Dementia
(294.10), Organic Delusional Disorder (293.81), Organic
Hallucinosi (293.82), Organic Mood Disorder (293.83),
Organic Anxiety Disorder (294.80), Organic Personality
20 Disorder (310.10), Organic Mental Disorder (294.80),
Obsessive Compulsive Disorder (300.30), Post-traumatic
Stress Disorder (309.89), Generalized Anxiety Disorder
(300.02), Anxiety Disorder NOS (300.00), Body Dysmorphic
Disorder (300.70), Hypochondriasis (or Hypochondriacal
25 Neurosis) (300.70), Somatization Disorder (300.81),
Undifferentiated Somatoform Disorder (300.70), Somatoform
Disorder NOS (300.70), Intermittent Explosive Disorder
(312.34), Kleptomania (312.32), Pathological Gambling
(312.31), Pyromania (312.33), Trichotillomania (312.39),
30 and Impulse Control Disorder NOS (312.39); Schizophrenia,
Catatonic, Subchronic, (295.21), Schizophrenia,
Catatonic, Chronic (295.22), Schizophrenia, Catatonic,
Subchronic with Acute Exacerbation (295.23),
Schizophrenia, Catatonic, Chronic with Acute Exacerbation
35 (295.24), Schizophrenia, Catatonic, in Remission
(295.55), Schizophrenia, Catatonic, Unspecified (295.20),
Schizophrenia, Disorganized, Subchronic (295.11),

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Schizophrenia, Disorganized, Chronic (295.12),
Schizophrenia, Disorganized, Subchronic with Acute
Exacerbation (295.13), Schizophrenia, Disorganized,
Chronic with Acute Exacerbation (295.14), Schizophrenia,
5 Disorganized, in Remission (295.15), Schizophrenia,
Disorganized, Unspecified (295.10), Schizophrenia,
Paranoid, Subchronic (295.31), Schizophrenia, Paranoid,
Chronic (295.32), Schizophrenia, Paranoid, Subchronic
with Acute Exacerbation (295.33), Schizophrenia,
10 Paranoid, Chronic with Acute Exacerbation (295.34),
Schizophrenia, Paranoid, in Remission (295.35),
Schizophrenia, Paranoid, Unspecified (295.30),
Schizophrenia, Undifferentiated, Subchronic (295.91),
Schizophrenia, Undifferentiated, Chronic (295.92),
15 Schizophrenia, Undifferentiated, Subchronic with Acute
Exacerbation (295.93), Schizophrenia, Undifferentiated,
Chronic with Acute Exacerbation (295.94), Schizophrenia,
Undifferentiated, in Remission (295.95), Schizophrenia,
Undifferentiated, Unspecified (295.90), Schizophrenia,
20 Residual, Subchronic (295.61), Schizophrenia, Residual,
Chronic (295.62), Schizophrenia, Residual, Subchronic
with Acute Exacerbation (295.63), Schizophrenia,
Residual, Chronic with Acute Exacerbation (295.94),
Schizophrenia, Residual, in Remission (295.65),
25 Schizophrenia, Residual, Unspecified (295.60), Delusional
(Paranoid) Disorder (297.10), Brief Reactive Psychosis
(298.80), Schizophreniform Disorder (295.40),
Schizoaffective Disorder (295.70), Induced Psychotic
Disorder (297.30), Psychotic Disorder NOS (Atypical
30 Psychosis) (298.90), Personality Disorders, Paranoid
(301.00), Personality Disorders, Schizoid (301.20),
Personality Disorders, Schizotypal (301.22), Personality
Disorders, Antisocial (301.70), and Personality
Disorders, Borderline (301.83)

35 As mentioned above, Compound I has useful
antipsychotic activity. This activity can be demonstrated
in models using well-established procedures. For

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example, the compound is assessed in a number of standard behavioral tests predictive of antipsychotic activity. Antagonism of apomorphine-induced climbing in mice is predictive of antipsychotic activity (see, Moore, N.A. et al. *Psychopharmacology* 94 (2), 263-266 (1988), and 96 539 (1988)). Further, the conditioned avoidance model, as described by Davidson, A.B. Differential Effect of Neuroleptic and other Psychotropic Agents on Acquisition of Avoidance in Rats, *Life Sci.* 18: 1279-1284 (1976).

One of the major pharmacological properties of currently employed clinical antipsychotic drugs in animals is their ability to block conditioned avoidance responding (Cook and Davidson, *Psychopharmacology, A Generation of Progress*, (Raven Press, New York: 1978) pp 563-567; Davidson and Weidley, *Life Sci.* 18:1279-1284, 1976).

There is a high correlation between their activity and potency on a conditioned avoidance test and their clinical efficacy and potencies as antipsychotic drugs (Creese et al, *Dopamine receptor binding predicts clinical and pharmacological properties of antischizophrenic drugs* *Science* 192:481-483, 1976).

In the conditioned avoidance test, animals learn to respond during a conditioned stimulus in order to avoid mild shock presentation. A response during the conditioned stimulus is termed an avoidance response, a response during shock is termed an escape response; a response failure is when the animal fails to respond either during the conditioned stimulus or the shock presentation and is indicative of motor impairment. Animals rapidly learn to avoid 99% of the time. Antipsychotic drugs decrease the percentage of avoidance without interfering with the ability of the animal to respond since the animals do emit escape responses. The percentage of response failures is considered a measure of motor impairment.

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Procedure.

Rats were required to press a response lever in an experimental chamber in order to avoid or escape foot-shock. Each experimental session consisted of 50 trials. During each trial, the chamber was illuminated and a tone presented for a maximum of 10 seconds. A response during the tone immediately terminated the tone and the houselight, ending the trial. In the absence of a response during the tone alone, tone plus foot shock (2.0 mA) was presented for a maximum of 10 seconds. A response during shock presentation immediately terminated the shock, the tone and the houselight, ending the trial.

Such studies suggest that Compound I may be especially desirable for the treatment of schizophrenia.

The following Examples are studies to establish the usefulness of the named compounds for treating such psychotic conditions.

Example 1**Human Clinical Trials**

The activity of Compound I for treating or alleviating psychosis can be demonstrated by human clinical trials. The study was designed as a double-blind, parallel, placebo-controlled multicenter trial. The patients are randomized into four groups, placebo and 3 other dosages of test compound. The dosages are administered orally with food. Patients are observed at four visits to provide baseline measurements. Visits 5-33 served as the treatment phase for the study.

During the visits, patients are observed for signs of agitation, mood swings, tremor, delirium, social withdrawal, and concentration abilities. These behaviors are indicative of the effect of the test compound on psychotic conditions.

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Treatment groups are compared with respect to the number and percent of patients who ever had the symptom during the double-blind portion of the study (visits 5 through 33), at a severity that was worse than during the baseline visits (1 through 4).

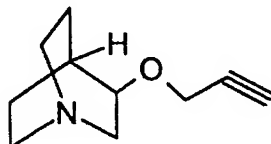
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We Claim:

1. A method for treating in a patient suffering
5 from a condition selected from the group consisting of
schizophrenia, schizophreniform disorder, and
schizoaffective disorder comprising administering to a
patient in need thereof, an effective amount of a Compound
I:

10 Compound I:

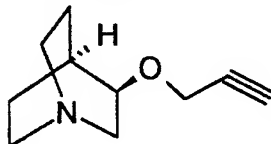


I

or

15 a pharmaceutically acceptable salt or solvate
thereof.

2. A method of Claim 1 wherein the Compound I is



20 3. A method of Claim 2 wherein the effective
amount is from 1 mg/kg to about 100 mg/kg per day.

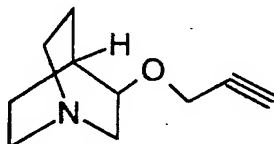
4. A method of Claim 1 wherein the effective
amount is delivered using a transdermal patch.

25 5. A method of Claim 4 wherein the transdermal
patch delivers from about 10 to about 100 mg of base
compound per day.

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6. A method of Claim 5 wherein the transdermal patch delivers an effective amount for one (1) to seven (7) days.

5 7.A method for treating in a patient suffering from a pathologic psychotic condition comprising administering to a patient in need thereof, an effective amount of a Compound I:



I

10 or a pharmaceutically acceptable salt thereof.

8. A method of Claim 7 wherein the pathologic psychotic condition is selected from the group consisting of
15 Conduct Disorder, Solitary Aggressive Type (312.00), Conduct Disorder, Undifferentiated Type (312.90), Tourette's Disorder (307.23), Chronic Motor Or Vocal Tic Disorder (307.22), Transient Tic Disorder (307.21), Tic Disorder NOS (307.20), Alcohol Withdrawal Delirium (291.00), Alcohol
20 Hallucinosi s (291.30), Alcohol Dementia Associated with Alcoholism (291.20), Amphetamine or Similarly Acting Sympathomimetic Intoxication (305.70), Amphetamine or Similarly Acting Sympathomimetic Delirium (292.81),
25 Amphetamine or Similarly Acting Sympathomimetic Delusional Disorder (292.11), Cannabis Delusional Disorder (292.11), Cocaine Intoxication (305.60), Cocaine Delirium (292.81), Cocaine Delusional Disorder (292.11), Hallucinogen Hallucinosi s (305.30), Hallucinogen Delusional Disorder (292.11), Hallucinogen Mood Disorder (292.84), Hallucinogen
30 Posthallucinogen Perception Disorder (292.89), Phencyclidine (PCP) or Similarly Acting Arylcyclohexylamine Intoxication (305.90), Phencyclidine (PCP) or Similarly Acting Arylcyclohexylamine Delirium (292.81), Phencyclidine (PCP) or Similarly Acting Arylcyclohexylamine Delusional Disorder

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(292.11), Phencyclidine (PCP) or Similarly Acting Arylcyclohexylamine Mood Disorder (292.84), Phencyclidine (PCP) or Similarly Acting Arylcyclohexylamine Organic Mental Disorder NOS (292.90), Other or Unspecified Psychoactive Substance Intoxication (305.90), Other or Unspecified Psychoactive Substance Delirium (292.81), Other or Unspecified Psychoactive Substance Dementia (292.82), Other or Unspecified Psychoactive Substance Delusional Disorder (292.11), Other or Unspecified Psychoactive SubstanHallucinosi

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sis (292.12), Other or Unspecified Psychoactive Substance Mood Disorder (292.84), Other or Unspecified Psychoactive Substance Anxiety Disorder (292.89), Other or Unspecified Psychoactive Substance Personality Disorder (292.89), Other or Unspecified Psychoactive Substance Organic Mental Disorder NOS (292.90), Delirium (293.00), Dementia (294.10), Organic Delusional Disorder (293.81), Organic Hallucinosi

Disorder (293.82), Organic Mood Disorder (293.83), Organic Anxiety Disorder (294.80), Organic Personality Disorder (310.10), Organic Mental Disorder (294.80), Obsessive Compulsive Disorder (300.30), Post-traumatic Stress Disorder (309.89), Generalized Anxiety Disorder (300.02), Anxiety Disorder NOS (300.00), Body Dysmorphic Disorder (300.70), Hypochondriasis (or Hypochondriacal Neurosis) (300.70), Somatization Disorder (300.81), Undifferentiated Somatoform Disorder (300.70), Somatoform Disorder NOS (300.70), Intermittent Explosive Disorder (312.34), Kleptomania (312.32), Pathological Gambling (312.31), Pyromania (312.33), Trichotillomania (312.39), and Impulse Control Disorder NOS (312.39);

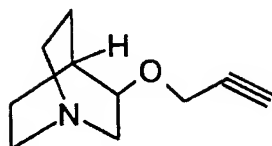
Schizophrenia, Catatonic, Subchronic, (295.21), Schizophrenia, Catatonic, Chronic (295.22), Schizophrenia, Catatonic, Subchronic with Acute Exacerbation (295.23), Schizophrenia, Catatonic, Chronic with Acute Exacerbation (295.24), Schizophrenia, Catatonic, in Remission (295.55), Schizophrenia, Catatonic, Unspecified (295.20), Schizophrenia, Disorganized, Subchronic (295.11), Schizophrenia, Disorganized, Chronic (295.12),

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Schizophrenia, Disorganized, Subchronic with Acute Exacerbation (295.13), Schizophrenia, Disorganized, Chronic with Acute Exacerbation (295.14), Schizophrenia, Disorganized, in Remission (295.15), Schizophrenia, Disorganized, Unspecified (295.10), Schizophrenia, Paranoid, Subchronic (295.31), Schizophrenia, Paranoid, Chronic (295.32), Schizophrenia, Paranoid, Subchronic with Acute Exacerbation (295.33), Schizophrenia, Paranoid, Chronic with Acute Exacerbation (295.34), Schizophrenia, Paranoid, in Remission (295.35), Schizophrenia, Paranoid, Unspecified (295.30), Schizophrenia, Undifferentiated, Subchronic (295.91), Schizophrenia, Undifferentiated, Chronic (295.92), Schizophrenia, Undifferentiated, Subchronic with Acute Exacerbation (295.93), Schizophrenia, Undifferentiated, Chronic with Acute Exacerbation (295.94), Schizophrenia, Undifferentiated, in Remission (295.95), Schizophrenia, Undifferentiated, Unspecified (295.90), Schizophrenia, Residual, Subchronic (295.61), Schizophrenia, Residual, Chronic (295.62), Schizophrenia, Residual, Subchronic with Acute Exacerbation (295.63), Schizophrenia, Residual, Chronic with Acute Exacerbation (295.94), Schizophrenia, Residual, in Remission (295.65), Schizophrenia, Residual, Unspecified (295.60), Delusional (Paranoid) Disorder (297.10), Brief Reactive Psychosis (298.80), Schizophreniform Disorder (295.40), Schizoaffective Disorder (295.70), Induced Psychotic Disorder (297.30), Psychotic Disorder NOS (Atypical Psychosis) (298.90), Personality Disorders, Paranoid (301.00), Personality Disorders, Schizoid (301.20), Personality Disorders, Schizotypal (301.22), Personality Disorders, Antisocial (301.70), and Personality Disorders, Borderline (301.83).

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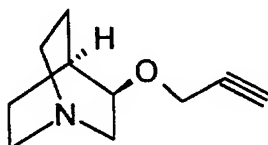
9. Use of a Compound I:



I

5 or a pharmaceutically acceptable salt or solvate thereof, optionally in combination with a pharmaceutically acceptable excipient, for the preparation of a pharmaceutical composition for treating a patient suffering from a condition selected from the group consisting of
10 schizophrenia, schizophreniform disorder, and schizoaffective disorder.

10. The use according to claim 9 wherein the Compound I is:



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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/07152

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61K 31/44

US CL : 514/305

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/305

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, STN (REGISTRY (STRUCTURE), CA, USPATFUL, WPIDS)

search terms: wal 2014, schizophrenia, psychosis

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,451,587 A (WALTHER et al) 19 September 1995, entire document.	1-10

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

28 MAY 1998

Date of mailing of the international search report

14 JUL 1998

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